Listing of Claims

The following listing of claims will replace all prior versions, and listings, of claims in the subject application:

Claims 1-6 (canceled).

7. (currently amended) A process for determining experimentally a plurality of three-dimensional atomic structures, each of which is associated with a corresponding protein, comprising the steps of:

(a) systematically organizing sequence information ~~for a plurality of proteins~~, ~~and any available~~ structural information and functional information for ~~the~~ a plurality of proteins into a database;

(b) clustering the plurality of proteins into a plurality of families using at least one bioinformatics tool and the sequence information, structural information and functional information stored in the database, wherein for each family, members of the family have homologous sequences, and said homologous sequences have similarity at approximately 30% identity or higher, with <0.001 probability of error;

(c) synthesizing for each family determined in step (b), in parallel simultaneously, a plurality of target proteins which are members of the family, using information stored in the database corresponding to the plurality of target proteins, and screening products of the synthesis to choose selected synthesized products, which are effective as the target proteins, for processing;

(d) preparing, purifying and characterizing each synthesized product that is chosen in step (c);

(e) crystallizing the processed synthesized product prepared, purified and characterized in step (d) to produce a plurality of specimen crystals, in parallel, of the target protein;

(f) testing the plurality of specimen crystals grown in step (e) for predetermined diffraction characteristics to determine

the specimen crystals which are suitable for diffraction measurement;

(g) performing high-throughput crystallography, including measuring for diffraction data the specimen crystals determined in step (f) to be suitable for diffraction measurement, building an atomic model of the target protein according to an analysis of the diffraction data, refining the model of the target protein against the diffraction data, and storing the refined model in the database;

(h) analyzing the refined model, stored in the database in step (g), of the target protein using sequence information corresponding to other family members which is stored in the database and structural information corresponding to other proteins which is stored in the database, and analyzing the refined model of the target protein for functional motifs and for surface characteristics;

(i) developing a homology model of one or more predicted protein structures using computational tools for homology model building and the refined model of the target protein retrieved from the database; and

(j) updating the database by using the at least one bioinformatics tool and the developed homology model to link the refined model of the target protein to other databases which store information concerning biological pathways and functional annotation,

wherein steps (f) through (j) are repeated for each of the other target proteins.

8. (previously presented) A process according to claim 7, further comprising the step of:

freezing the specimen crystals of the target protein which are determined in step (f) to be suitable,

wherein the suitable specimen crystals are frozen before being measured for the diffraction data in step (g).

9. (previously presented) A process according to claim 7,

wherein

step (c) includes cloning for each family determined in step (b), in parallel, cDNAs corresponding to the appropriately representative family members into a plurality of expression vectors for a plurality of expressions systems,

constructs obtained in the cloning are screened for expression to determine the ones that are effective as proteins, and

the expressed proteins determined to be effective are processed in step (d).

10. (previously presented) A process according to claim 7, wherein

the high-throughput crystallography in step (g) is performed using a synchrotron storage ring having undulator beamlines along with a multiwavelength anomalous diffraction method, and

the diffraction data measured in step (g) is analyzed using a multiwavelength anomalous diffraction phasing method.

11. (previously presented) A process according to claim 10, wherein selenomethionine is incorporated in the plurality of target proteins synthesized in step (c), and the multiwavelength anomalous diffraction phasing method is used to analyze diffraction data measured for selenomethionyl proteins.

12. (previously presented) A process according to claim 7, further comprising the step of

using the homology model developed in step (i) in at least one of target selection, drug design, and design of constructs for experimental analysis.

13. (currently amended) A process for determining three-dimensional macromolecular atomic structures, said process including the following steps:

(a) ~~maintaining a database of~~ organizing known structural information, including structures determined by the

process and other known structures, ~~including~~ into a database, and updating the database with additional structural, sequence, and/or functional information as the additional structural, sequence, and/or functional information is acquired;

(b) using bioinformatics tools to cluster known gene products into families of homologous sequences, said homologous sequences having similarity at approximately 30% identity or higher, with <0.001 probability of error;

(c) cloning, for each family of homologous sequences determined in step (b), in parallel simultaneously, cDNAs from selected species into expression vectors for one or more expressions systems;

(d) screening for expression constructs obtained from said cloning in step (c);

(e) preparing, purifying and characterizing expressed proteins obtained from step (d);

(f) crystallizing purified proteins obtained from step (e), in parallel, against crystallization screens;

(g) testing crystals obtained from step (f) for predetermined diffraction characteristics, to determine suitable crystals;

(h) freezing a suitable crystal obtained from step (g), and measuring the frozen crystal for diffraction data, by using a multi-wavelength anomalous diffraction method at a synchrotron storage ring which uses beamlines for high-throughput crystallography;

(i) analyzing the diffraction data obtained from step (h) by using a multi-wavelength anomalous diffraction phasing method, building an atomic model, and refining the atomic model against the diffraction data;

(j) analyzing the refined model obtained from step (i), ~~by using~~ in a context of sequence information from other family members and ~~by using~~ in a context of information of other structures, and analyzing for functional motifs and for surface characteristics to define active sites

and macromolecular contact sites;

(k) using information obtained from step (j) to define classes of compounds predicted to have binding potency;

(l) developing homology models by using homology model building tools along with the refined model obtained from step (i); and

(m) using the homology models obtained from step (l) for target selection, drug design, and/or design of constructs for experimental analysis.